HOW DID I GET SO LATE SO SOON? A REVIEW OF
TIME PROCESSING AND MANAGEMENT IN AUTISM

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ABSTRACT

While the definition of Autism Spectrum Disorder (ASD) does not include any explicit criteria concerning difficulties of time perception or management, there is growing evidence of atypical temporal perception in individuals with ASD. This review synthesizes the evidence and gaps of the current literature on time processing in ASD. After a brief overview of clinical findings and available assessment tools, we synthetize outcomes of studies evaluating time perception at second and infra-second level, and then, recent literature on the circadian timing system. Findings point that all levels
of time processing are atypical in autism (i.e. millisecond, interval and circadian timing). We discuss how time perception abnormalities and ASD core symptoms might intertwine and offer a new perspective for future research on this topic. We advocate the need to systematically assess temporal perception in ASD, and to include these aspects in global functional assessments before intervention. Implementing early intervention techniques to remediate time perception alterations in children with ASD may substantially improve their developmental trajectory.

**KEYWORDS:**
Autism; Time processing; Circadian rhythm; Remediation; Time assessment

**INTRODUCTION**
Autism spectrum Disorder (ASD) is a common and life-long neurodevelopmental disorder characterized by difficulty with communication and social interaction and stereotyped, repetitive behaviors. Cognitive functioning is highly heterogeneous across individuals with ASD. ASD generally appears in the first two years of life (American Psychiatric Association, 2013). Current classifications of the core diagnostic criterion in ASD include atypical sensory and perception behaviors. However, despite being emphasized upon by clinicians and researchers, time management and perception atypicalities are not included in those criterion (Stevenson et al., 2016; Wing, 1996). Nonetheless, temporal issues in ASD are observed in daily clinical practice. Moreover, several recent studies have reported that a significant proportion of cognitive processes involve the encoding and precise treatment of temporal information (Allman & Mareschal, 2016; Christine M. Falter, Elliott, & Bailey, 2012a; Lambrechts, Falter-Wagner, & van Wassenhove, 2018). Some authors have even suggested that deficits in time processing could be central to the pathological pathways leading to ASD phenotypes (Allman, 2011a; Allman & Mareschal, 2016; Allman, Pelphrey, & Meck, 2012). It is possible then, that a “temporal” point of view could lead to a better understanding of the neurodevelopment pathways found in ASD and help to develop new early targeted interventions to improve the prognostic of this disorder.

Time processing is a broad construct. During the last decade, a consensus has emerged to differentiate between three kinds of time measurement, each having different neural mechanisms involved: circadian, interval and millisecond timing (Buhusi & Meck, 2005). **Circadian timing** intervenes on a 24-hour based duration and allows control of sleep-wake rhythms. This system is present in a multitude of different species. In humans, it is regulated by the supra-chiasmatic nucleus, which detects perceived light, to synchronize diurnal and nocturnal behaviors with day-night alternations (Panda, Hogenesch, & Kay, 2002). **Interval Timing** operates within a spectrum spanning from less than one second to a few minutes and refers to conscious time estimation. It is involved in the decision-making
processes. The precise neural mechanisms involved in interval timing are currently under debate, yet there is strong evidence for the implication of cortico-striatal networks and dopamine neurons. **Millisecond Timing** refers to the measurement of time by intervals of under one second and contributes to crucial functions such as motor control and speech. Millisecond timing relies on different cerebral structures depending on the sensory modality. For example, the cerebellum is involved in motor control (De Zeeuw et al., 2011), and the auditory cortex participates in speech processing (Nourski & Brugge, 2011).

This review aims to discuss the current scientific literature about time processing in ASD, at its different levels. We present an overview of recent scientific data and knowledge gaps on time processing in ASD compared to individuals with a typical development (TD).

For this purpose, we searched for articles on PubMed and PsycINFO databases and included studies or reviews written in English and French, published between 1980 and 2019. Articles were searched using a combination of keywords related to ASD, time processing, synchrony or order judgment, circadian time and time assessment. After the removal of duplicate articles, a first selection was then made based on screening title and abstract by one of the authors (LJ). Full-texts were then read and classified according to their main topic (time perception, circadian time or clinical assessment), and reference lists were also screened for additional relevant papers to insure completeness. Beginning with a total of 1074 articles, 298 were excluded as duplicates, 776 were screened on title and abstract, 605 were excluded (not related to time processing or circadian system, wrong study population, case report...) and 171 full-text articles were ultimately included in the review.

**ASD AND TIME PROCESSING: CLINICAL OVERVIEW**

Time processing is an important but neglected feature of ASD, as much in its clinical definition as in daily practice. Few clinicians have reported or assessed this feature as essential for daily adaptive behavior. It has been reported that participants with ASD without Intellectual disability (i.e. with IQ superior or equal to 70) have difficulties making chronological sense of their memories (Bennetto, Pennington, & Rogers, 1996). Adults with ASD also reported a lack of sense of time, and difficulty understanding continuity in time, even in their own personal history (Vogel et al., 2019). While telling time on a clock was not a problem for them, they mentioned difficulty in associating specific hours to related activities, or in managing the allotted time for that activity (J. Boucher, 2001). Clinical studies are also limited. Two parent-report studies showed a significant alteration in time perception in ASD children compared to typically developing children (Allman & Wearden, 2011), and also encountered difficulties thinking in a diachronic fashion (i.e. to think about past or future stages of a current situation) or in considering successive discrete events as being part of a whole (Jill Boucher, Pons, Lind, & Williams, 2007).

Two other authors indirectly reported time difficulties. One suggested that repetitive behaviors could be an effective way for people with ASD to create a sense of rhythmicity where there is none exists (Tordjman et al., 2015). A qualitative study, including the statements of 26 adult participants with ASD, indicated that routine and repetitive behaviors were used to accentuate the impression of fading time and prevent from the impression of “interrupted time” (Vogel et al., 2019). Indeed, those symptoms could reflect compensating mechanisms used to bypass inefficient time processing. Studies evaluating
the correlation between time perception and the severity and frequency of those repetitive symptoms could help understand the relationship between these two features.

In parallel with the thin “clinical” literature about time perception difficulties, there are few tools available to measure time management and processing. Some well-known tests, developed to measure daily adaptive behavior, have included few/minimal items for evaluating time perception. For instance, the Vineland Adaptive Behavior Scales (VABS-II; (Sparrow, Cicchetti, & Balla, 2005)), is a scale scored by a clinician while interviewing a caretaker or filled in by caretakers themselves. It includes items pertaining to time reading on analog or digital devices, and an observance of appointments and schedules. These items are included under a broader construct named “Community,” which pertains to skills necessary for interacting with and navigating in the community (such as money management, use of a telephone, autonomy in taking public transportation, etc.). However, since these items are not aggregated in a separate dimension, one cannot derive a standardized score indexing time perception from such a tool.

One team designed a specific tool in order to assess time perception in children with disabilities aged 5 to 10 years old, the Kit for assessing Time Processing Ability (KaTid) (G. Janeslätt, Granlund, Alderman, & Kottorp, 2008; Gunnel Janeslätt, Granlund, & Kottorp, 2009). The tool assesses three dimensions: time perception (experiencing and assessing the length and passage of time, including interval timing), time orientation (awareness of the day, date, month and year, as well as the ability to situate events in a timeline), and time management (the ability to prioritize one task among others, to order a set of tasks, and to allocate the optimum amount of time to each task). The latter dimension seems to develop at a later age according to one study (i.e. between seven and nine years old; (Gunnel Janeslätt, Granlund, Kottorp, & Almqvist, 2010) and has been theorized to rely on the development of the first two dimensions (G. Janeslätt, 2012). The tool includes 51 items in the form of a combined visual and verbal presentation for allowing assessment of children with communication or reading impairments. Depending on the item, the child answers verbally or by pointing at a picture. It is of note that the validation study for this tool is in favor of a unidimensional construct (named Time Processing Ability), thus limiting the conclusions that can be drawn on the effects restricted to one or two dimensions. A version for older children and adolescents aged 10 to 17 years old (the KaTid-Youth) has also been designed by the same team (G. Janeslätt, 2012; Wennberg, Janeslätt, Kjellberg, & Gustafsson, 2018).

The same team designed a self-rated questionnaire for parents to assess their child’s time management ability (Parent Scale of the Child’s Time Management in Daily Life; (G. Janeslätt et al., 2008; Gunnel Janeslätt et al., 2009)). This scale includes 13 items investigating various aspects of time perception, from the adherence to a regular sleep-wake pattern to the ability to use calendars and clocks. KaTid and the Parent Scale have been found to be highly correlated in several studies (G. Janeslätt et al., 2008; Gunnel Janeslätt et al., 2009).

A self-rated questionnaire for children aged from 10 to 17 years old was also designed (the Time S questionnaire; (Sköld & Janeslätt, 2017)). The questionnaire includes 21 statements which are rated with a Likert-like frequency scale, with four response alternatives. It is of note that scores from this questionnaire were not significantly correlated with scores from the KaTid-Youth in the validation study (Sköld & Janeslätt, 2017), which raises questions about children and adolescents with disabilities
assessing their own time management capacities reliably, and/or casting doubt upon the fact that both tools (the KaTid and the Time S) measure the same construct.

These questionnaires could improve clinical assessment of time perception. Information on temporal perception and processing in ASD could be add to global functional assessments. This could lead to a better understanding of time perception difficulties impact in daily life. But if a clinical perspective is important, a view of cognitive mechanisms may allow a better understanding of clinical observations.

“Millisecond” and “interval timing” in ASD

Interval timing: A deficit induced by atypical but modifiable cognitive strategies?

Many different approaches exist to evaluate interval timing (Grondin, 2010). In ASD research, the majority of experiments have used temporal reproduction tasks (where the subject is asked to reproduce a standard interval of time by manipulating a device, e.g. pressing a button or pulling a lever) and temporal comparison tasks (where the subject is asked to compare two intervals of time and to indicate if these intervals are similar or not). Other experiments use a temporal bisection task, in which subjects are asked to compare temporal stimuli to two references, between a “long” and “short” stimuli. After being trained on the reference stimuli, probe stimuli are then introduced. The subject must indicate with which reference stimulus they believe the probe stimulus is most similar to, the long or the short one. From the data collected during the task experimenters are able to construct a psychometric curve. This curve shows the point of indifference (i.e. the stimulus length at which participants show a 50/50 chance of picking the long or short reference), offering insight on how time is represented and processed (Kopec & Brody, 2010).

Using this framework, Szelag et al. first demonstrated a very clear alteration of precision and accuracy in temporal reproduction tasks in children with ASD compared to typically developing controls (TD), with an overestimation of a longer duration and an underestimation of a shorter duration in ASD group (Szelag, Kowalska, Galkowski, & Pöppel, 2004) (N = 14; 7 ASD and TD, average age of 12 years).

Similar results have been found in several studies during the last two decades and a synthesis is presented in Table 1. Most of the studies found a significant difference in interval timing processing in ASD group compared to typically developing controls, with ASD individuals showing higher detection thresholds (relating to the minimum interval between sequential stimuli needed for individuals to perceive an interruption between the stimuli) (Bhatara, Babikian, Laugeson, Tachdjian, & Sininger, 2013; Foss-Feig, Schauder, Key, Wallace, & Stone, 2017; Isaksson et al., 2018; Karaminis et al., 2016; Lambrechts, Falter-Wagner, & van Wassenhove, 2017), less accurate and more variable responses on duration reproduction (Brenner et al., 2015; Martin, Poirier, & Bowler, 2010; Salunkhe et al., 2018) or poorer sensitivity to duration on a temporal bisection task (Allman, 2011b; Brodeur, Green, Flores, & Burack, 2014). Decrease in auditory gap detection abilities were associated with lower phonological processing scores but also weaker receptive language skills (Foss-Feig et al., 2017) or higher communication impairment score (Christine Michaela Falter, Noreika, Wearden, & Bailey, 2012). Autistic traits in a TD population, as measured by the Autistic Quotient (Ruzich et al., 2015) were found
to be positively correlated to duration discrimination thresholds, extending the applicability of this finding to the broader autistic spectrum (Stewart, Griffiths, & Grube, 2018).

Table 1 about here

In contrast, some studies failed to report differences between ASD and control groups concerning interval timing (Edey, Brewer, Bird, & Press, 2019; Gil, Chambres, Hyvert, Fanget, & Droit-Volet, 2012; Jones et al., 2009; Jones, Lambrechts, & Gaigg, 2017; Mostofsky, Goldberg, Landa, & Denckla, 2000; Wallace & Happé, 2008).

Maister and al. suggested that these contradictions could be explained by the variety of measurement methods. Starting from this hypothesis the authors tried to assess temporal processing on a large spectrum of various duration in children with and without ASD in a procedure that addressed the methodological concerns associated with previous research. The study was divided into two experiments. The first one was conducted with 42 children (21 with ASD and 21 TD, 8-13 years-old, normal IQ) for several durations (0.5, 1, 2, 4, 10, 30, and 45 seconds). Each duration was evaluated twice in order to measure variability between the first and the second trial for each subject, which could reflect changes in attentional levels. The results showed a statistically significant alteration in temporal reproduction abilities, but only for very short (0.5, 1 and 2 seconds) or very long (45 seconds) periods of time. The inter-subject variability showed an attentional bias for short to average durations (0.5, 1, 2, 4 and 10 seconds) in subjects with ASD. For longer duration, a positive correlation between duration reproduction accuracy and short-term memory capacity was demonstrated (Maister & Plaisted-Grant, 2011) and was confirmed in another study (Brenner et al., 2015). Those results suggest that, in order to perform temporal judgements, individuals with ASD use different cognitive strategies (and different neural substrates) compared to TDC individuals.

Consistent with this conclusion, a recent comparative MEG study (19 subjects with ASD and 19 TD) using an auditory temporal comparison task confirmed the attentional deficit presented by ASD subjects for short duration discrimination (Lambrechts et al., 2018). Participants were told to evaluate either the length (300, 600 or 900ms) or the pitch (490 Hz, 500 Hz or 510 Hz) of a target stimulus compared to a standard stimulus. A significant deficit in sensitivity to temporal duration was found in subjects with ASD compared to controls. In MEG evaluations, auditory evoked responses elicited by the presentation of the standard stimulus in duration tasks were different between groups. ASD presented a significantly longer neuronal response to the standard stimuli, going beyond its actual length. A slower decrease in MEG activity after the end of the sound was also reported. These results might indicate that from the standard stimulus a less precise encoding of the offset may be found in ASD, underlying the diminished sensitivity to duration.

Additionally, because of the very nature of pitch and duration, pitch discrimination could be resolved shortly after the onset of the tone, whereas duration comparison could only be resolved after the offset of the tone. Participants with ASD presented an enhanced and sustained evoked response to the pitch instruction whereas their evoked response to duration instruction were diminished and imprecise. The opposite pattern was found in control participants. These results suggest that ASD participants, unlike TD controls, do not allocate the relevant attentional resources to the processing of the target duration.
In terms of cortical regions, different activation patterns were found between ASD and TD groups. In the control group, MEG evoked responses for duration were significantly higher in the right hemisphere although responses for pitch were higher in the left hemisphere. In the ASD group, brain activation was similar in the left and right hemispheres regardless of the given instructions, pointing toward a less differentiated allocation of neural resources in ASD.

Therefore, there is growing evidence of an impairment of interval timing in ASD. Scientific literature emphasizes ASD’s atypical cognitive strategies when processing time. Attentional functions and short-term memory may be implied in this impairment and could be targeted by cognitive remediation. Though, a mediation analysis evaluating the benefits of cognitive remediation on interval timing in relation to attention or memory could be of great use in the understanding of the interval timing process.

Arguments for impairment in specific sensory modalities

Certain authors have suggested that differences in processing of visual information in people with ASD explains the heterogeneity of the results found in the literature concerning time processing. They have argued that processing visual time information might be preserved, or even improved, in subjects with autism, while processing information in other sensory (particularly auditory) modalities might be degraded (Edey et al., 2019; Christine M. Falter, Elliott, & Bailey, 2012b; Foss-Feig et al., 2017).

For instance, using a visual temporal bisection task, no difference was found between ASD and TD participants (Gil et al., 2012; Jones et al., 2017), even in populations with auditory temporal processing impairment (Foss-Feig et al., 2017; Kwakye, Foss-Feig, Cascio, Stone, & Wallace, 2011). More importantly, several authors reported enhanced time processing performance of ASD subjects with the use of visual tasks (Edey et al., 2019; Christine M. Falter et al., 2012b; Karaminis et al., 2016).

A neuroimaging study also supports this hypothesis (Lukito et al. 2018). A visual duration discrimination task showed no difference in terms of performance between TD, ASD, Attention Deficit/Hyperactivity disorder (ADHD) or co-morbid ASD and ADHD young adults. The authors demonstrated a neurofunctional deficit in the typical duration discrimination brain region, when comparing ASD+ADHD group to ASD only or TD, but not to ADHD only. ASD only groups didn’t show any significant difference in cerebral activation patterns.

To conclude on this section, it appears that time perception is dependent on sensory modality. Based on their preserved-to-enhanced visual capacities, individuals with ASD seem to be efficient in measuring time through visual cues. But because of anomalies in auditory processing, time perception is altered when relying on auditory cues. It remains to be studied how other modalities with good temporal resolution (such as touch or even interoceptive modalities) are affected in ASD. It is also interesting to note that this data fits within the empirical clinical practices, in which visual aids are used to help ASD individuals to better represent time intervals and schedules. It could be interesting to design studies profiling ASD individuals on their visual and auditory capacities, and then assessing their responses to visual aid interventions.

Autism and multimodal temporal integration
There are an accumulation of studies supporting the hypothesis of impairment in multisensory integration in ASD (Chan, Langer, & Kaiser, 2016; Feldman et al., 2018; Stevenson et al., 2016). This capacity is based on multimodal temporal integration, which is the capacity of the central nervous system to temporally integrate different external events (perceived by different sensory modalities) into a single percept. This cerebral capacity is notably involved in the McGurk effect (McGurk & Macdonald, 1976). In this illusion, a manipulated video shows a speaker saying the syllable “ga” while an audio clip produces the syllable “ba”, leading viewers to hear “da” or “that” syllables.

Temporal integration is important in everyday life, as illustrated by the case of patient AWF (Hamilton, Shenton, & Branch Coslett, 2006). Following a brain injury of unknown etiology associated with bilateral parietal hypoperfusion, AWF started perceiving what he heard and saw as being unsynchronized, like “watching a movie with the audio out of sync”. Interestingly AWS was incapable of perceiving the McGurk effect. He coped with this asynchrony by limiting face-to-face conversations and looking away during conversations, which could give the impression of social avoidance.

The past twenty years of research has revealed impairment in temporal integration in subjects with ASD, with a notably decreased susceptibility to the McGurk effect (de Gelder, Vroomen, & Van der Heide, 1991; E. G. Smith & Bennetto, 2007; Stevenson et al., 2014; Williams, Massaro, Peel, Bosseler, & Suddendorf, 2004) or worsened judgement of simultaneity in an audiovisual task (de Boerschellekens, Eussen, & Vroomen, 2013; Foxe et al., 2015; Noel, Niear, Stevenson, Alais, & Wallace, 2017; E. Smith, Zhang, & Bennetto, 2017).

Atypical patterns of cerebral connectivity are proposed as neurobiological foundations of those temporal integration impairments (Martínez-Sanchis, 2014), with hyper-connectivity in some unimodal sensory regions, such as visual cortex, while hypo-connectivity between sensory region and attentional network is reported. Those particular patterns are correlated to ASD severity (Martínez et al., 2019).

Temporal processing abnormalities are probably not the sole ontogenetic cause of ASD but subtle impairments in low-level neuronal functions could have cascading effects on the development of higher-level functions (Stein & Stanford, 2008). An association between impaired temporal processing mechanisms and other cognitive functions (such as social cognition, language processing and understanding of causality) support this hypothesis (Christine Michaela Falter et al., 2012; Foss-Feig et al., 2017). Increased audiovisual integration in individuals with ASD has been associated with better language, communication abilities and reduced autism symptom severity (Feldman et al., 2018), emphasizing the importance of this mechanism in neurodevelopment.

Going a bit further, Stevenson et al. recently proposed a mediation analysis to explore the eventual causality of temporal processing impairment on speech perception. Through a series of tasks assessing multisensory temporal processes, multisensory integration and speech perception in children with and without ASD, the authors demonstrated that the relationship between temporal processing and speech perception was significantly mediated by abilities to correctly integrate social information across auditory and visual modalities (Stevenson et al., 2018).

Indeed, alteration of multimodal temporal integration in ASD is a robust finding, mostly concerning audio-visual integration. This impairment is linked with higher-cognitive skills dysfunction, such as language comprehension. Imagery studies are a new step in multimodal temporal integration studies,
focusing on regions of cerebral sensory connectivity. Combined functional imagery with cognitive tasks for multimodal temporal integration will provide further evidence of ASD neurobiological particularities.

Considerations for future studies

At this point, there is growing evidence of an alteration in temporal processing in ASD at different levels: duration estimation, temporal reproduction and simultaneity judgement, leading to multimodal temporal integration impairment, in turn leading to cascading effects on time management, speech processing and possibly on repetitive behavior. Nevertheless, because of the heterogeneity in the design of the studies and the small sample sizes, cross-study comparisons should be done with caution. Several factors must be considered in the designing of future ASD time processing studies.

Given that ASD is a neurodevelopmental disorder, a particular attention should be given to the developmental age. Performance in interval reproduction is highly related to developmental age in TD (Sciutti, Burr, Saracco, Sandini, & Gori, 2014) and ASD subjects have shown altered performances compared to age matched TD, and comparable to younger TD (Karaminis et al., 2016). Concerning temporal multisensory integration, impairment displayed in young ASD children tends to normalize by adulthood, with adolescence being the pivotal point of transition (Beker, Foxe, & Molholm, 2018).

In addition, as the term “spectrum” indicates, the ASD population is highly heterogeneous regarding symptomatology. Recent diagnostic classifications highlight the differences in clinical presentations in terms of cognitive or behavioral competencies (American Psychiatric Association, 2013). Impairments in ASD could be preeminent in some domains and absent in others, such as communication, socialization, repetitive behavior, etc. Overall severity does not reflect the diversity of the ASD phenotype and scale subscores are necessary to evaluate the different domains of difficulties. Subgrouping individuals (including non-clinical participants with autistic traits) according to their clinical and cognitive profile is required to better understand the sources of discrepancies between reported data.

Cognitive function deficits and potential intellectual disabilities, frequently associated with ASD, could also be confounding factors (Brodeur et al., 2014). Observed deficits might reflect cognitive limitations as non-autistic subjects with ID also have difficulties in perceiving and processing time (Haldemann, Stauffer, Troche, & Rammsayer, 2012; Rammsayer & Brandler, 2007). To date, the available corpus of data does not allow for the comparison between ASD with or without ID and no studies have been designed for this purpose. A deficit in short-term memory, visuo-spatial abilities or attentional system, which are highly related to temporal processing (Allman, DeLeon, & Wearden, 2011; Bauermeister et al., 2005; Brenner et al., 2015; Maister & Plaisted-Grant, 2011) should be controlled.

ADHD, another frequent comorbidity in ASD (Ghirardi et al., 2018), has been largely studied in the “temporal processing” field. Individuals with ADHD exhibit a strong alteration of time duration perception and temporal judgement (Hart, Radua, Mataix-Cols, & Rubia, 2012; Toplak, Dockstader, & Tannock, 2006). As presented above, Lukito et al. found significant differences in brain activity during temporal processing tasks in ASD+ADHD subgroups but not in the ASD only subgroup (Lukito et al., 2018). A recent study confirmed those results and reported an alteration in temporal reproduction in ADHD and ADHD+ASD groups, but not in ASD only group (Salunkhe et al., 2018). Indeed, ADHD
symptoms may have an impact on the temporal processing tasks and should be considered when studying temporal performances in ASD.

Lastly, it should be noted that prescriptions are seldom represented in population characteristics. Even if no pharmacological treatment is actually recommended in ASD, neuroleptics and stimulants are commonly prescribed to subjects with ASD. It has been proposed that time processing mechanisms are based on the dopaminergic system (Lewis & Miall, 2006; Soares, Atallah, & Paton, 2016). It is then mandatory to control related medications, such as haloperidol or methylphenidate, which have been implicated in timing performances (Soares et al., 2016; Toplak et al., 2006).

CIRCADIAN TIME

Circadian time has a very different temporal scale than the previously stated mechanisms of time measurement. As will be discussed in this section, recent research has emphasized the potential disruption of circadian rhythms in individuals with ASD.

What is “circadian time”?

Circadian time is a near-24-hour cycle present in mammalian species. While it is genetically coded, the period, phase and amplitude of the cycle is influenced by many other environmental factors, such as light exposure and social cues, and by endogenous factors, such as physical activity. The circadian cycle is managed by a general clock located in the supra-chiasmatic nucleus (SCN). This pacemaker sets the time using neuronal activity, body temperature and hormonal secretions; one of the major hormones being melatonin. Melatonin results from the enzymatic transformation of serotonin, synthesized in the pineal gland during the night. As a biological signal of light/dark cycles, this hormone is an important synchronizer of human physiology (Pagan et al., 2014; Pagan et al., 2017). In the periphery, independent clocks are found in different organs, regulated by varying external factors and then re-synchronized by the SCN (Logan & McClung, 2019; Marco, Velarde, Llorente, & Laviola, 2015). At the cellular level, this timing is set by a complex molecular clock composed of transcriptional-translational feedback loops driven by CLOCK and BMAL1 genes (Geoffray et al., 2016; Marco et al., 2015; Schuch, Genro, Bastos, Ghisleni, & Tovo-Rodrigues, 2018).

In human development, there is evidence that the circadian system forms as early as the 18th week of gestation, with the emergence of melatonin receptors in fetal SCN (Logan et al., Jin et al., Marco et al.). Melatonin, which is known to pass through the placenta and the blood-brain barrier, at this time of development is probably the main relay of time-of-day information via the increase of circulating maternal melatonin (Jin, Choi, Won, & Hong, 2018; Logan & McClung, 2019). In full-term infants, temperature rhythms appear immediately after birth, whereas other rhythms (including rest–activity, sleep–wake and hormonal cycles) typically develop between 3 and 6 months of age (Logan & McClung, 2019).

In homeostasis, the circadian system modulates multiple functions, such as the sleep/wake cycle, feeding schedules, and body temperature. The hormones involved, notably melatonin, also have antioxidative functions, which are important to brain development. Moreover, the genes involved in these processes are known to manage various significant bodily activities such as neurogenesis,
cortical development, neurotransmission, synaptic homeostasis, neuronal metabolism and oxidative stress (Charrier, Olliac, Roubertoux, & Tordjman, 2017; Logan & McClung, 2019).

Dysfunction of such an essential regulatory system has obvious severe pathological behavioral consequences and may also be implicated in pathological neurodevelopmental pathways.

Evidence of impaired circadian rhythm in ASD

It is well known that sleep disorders are heavily linked to circadian rhythm dysfunction and are more frequent in children with ASD than in neurotypical children (Díaz-Román, Zhang, Delorme, Beggiato, & Cortese, 2018; Tordjman et al., 2012). Different types of sleep issues are found in ASD; anxiety related to falling asleep, higher sleep-onset delay, and circadian rhythm disturbances are more frequent in children with ASD compared to those with general intellectual disability (Geoffray et al., 2016; Jin et al., 2018; Reynolds et al., 2019). Compared to controls without neurodevelopmental disorders, a decrease in total sleep duration and a greater percentage of night-awakenings are reported in ASD between 30 months of age into adolescence (Díaz-Román et al., 2018; Elrod & Hood, 2015; Humphreys et al., 2014). Recently reported is a prevalence of sleep disturbance, particularly during early life, occurring at a rate between 64% - 93% or a recent systematic review, see (Carmassi et al., 2019). In terms of sleep patterns, recent literature shows evidence of increased rapid eye movement (REM) sleep latency, immature organization of REM sleep or a decreased total of REM sleep associated to an increased proportion of stage 1 sleep (Díaz-Román et al., 2018; Maruani et al., 2019). These sleep issues are present from young age to adulthood and tend to increase with ASD severity (Adams, Matson, Cervantes, & Goldin, 2014).

Different underlying pathways have been explored to account for these observations. The most robust account relates to the decrease in melatonin levels in ASD compared to controls (Geoffray et al., 2016; Logan & McClung, 2019; Maruani et al., 2019; Melke et al., 2008; Pagan et al., 2014). The decreased levels may result from an alteration of the enzymatic pathway (composed of acetylserotonin methyltransferase (ASMT) and arylalkylamine N-acetyltransferase (AANAT)) which drives the conversion of serotonin into melatonin (Carmassi et al., 2019).

At a behavioral level, sleep disorders and decreased levels of melatonin appear to be correlated to specific symptoms in ASD. In two different studies, Tordjman et al. (Tordjman et al., 2012; Tordjman, Anderson, Pichard, Charbuy, & Touitou, 2005) observed a negative correlation between the excretion of 6-SM (a melatonin urine metabolite) and the repetitive use of objects. Lower melatonin excretion was also significantly associated with social communication impairments, especially for verbal communication and social imitative play, which are core symptoms of ASD (American Psychiatric Association, 2013). Furthermore, a decrease of autistic symptoms (such as social withdrawal, stereotyped behaviors or communication dysfunction) after the administration of melatonin strengthens the hypothesis of the role of the circadian system in ASD physiopathology (Malow et al., 2012; Tordjman et al., 2015).

At a genetic level, dysregulation of circadian rhythm pathway genes is also reported in ASD (Bourgeron, 2007; Hu et al., 2009; Nicholas et al., 2007; Olde Loohuis et al., 2017; Yang et al., 2016) and linked to autism severity (Hu et al., 2009).
To better understand the cascading consequences of this complex physiopathology, Vilches et al. (2014) and Smarr et al. (2017) analyzed the effect of constant light exposure during pregnancy on the circadian genes and behavior in mice offspring. The results showed that light induced maternal circadian disruption, generating an alteration in circadian gene expression in the hippocampus of their offspring. This alteration was associated with long-lasting spatial memory dysfunction, an increase in stereotyped behaviors and a decrease in social activities. More interestingly, pregnant mice exposed to constant light but given a melatonin supplement, corrected the previously described gene alterations and led to normal development of the offspring (Vilches et al. 2014).

In summary, the circadian rhythm pathways is altered in ASD at different levels. Indeed, an overall decrease in melatonin levels, a dysfunction of melatonin enzyme pathways and a dysregulation of circadian genes are reported, not only with sleep/wake disorders but also linked to an increase in autistic symptoms and cognitive dysfunctions. Yet, even if several studies are available, none of them offer a global view on the circadian system.

Future studies should assess circadian system alterations at multiple levels but also their interdependence (from clock genes, to plasmatic level of melatonin and electrophysiological sleep markers) on well characterized ASD populations. This could allow a better identification of mechanisms explaining circadian rhythm dysfunction in autism.

Developmental implications of an impaired circadian rhythm: a bidirectional hypothesis

A WRONG TIMING IN PLASTICITY ONSET

Tordjman et al. (2015) hypothesized that given the major role of melatonin in the ontogenetic establishment of diurnal rhythms, the synchronization of peripheral oscillators (also termed “clocks”) and the regulation of human circadian rhythms, melatonin might also be involved in the synchrony of motor, emotional, and relational rhythms which are crucial in the early development of social communication.

More recently, Kobayashi et al. (2015) found evidence for the implication of circadian genes in the timing of brain development (Kobayashi, Ye, & Hensch, 2015). Notably, they demonstrated that circadian clock genes could control the onset of a critical period of plasticity in the neocortex by acting on GABAergic interneurons expressing the calcium binding protein parvalbumin (PV+ cells). PV+ cells constitute an essential factor in neuronal plasticity, particularly by maintaining the excitation/inhibition balance, which may be dysfunctional in ASD (Butt, Stacey, Teramoto, & Vagnoni, 2017). It was also recently reported that PV knockout mice (PV−/−) or heterozygous (PV+/−) mice display behavioral phenotypes in accordance with all core symptoms present in human ASD individuals (Wöhr et al., 2015). Moreover, in their meta-analysis, Gogolla et al. found a PV-cell decrease in the neocortex across multiple ASD mouse models and further replicated the results in a chemical and a genetic model of ASD (Gogolla et al., 2009).

Considering the importance of brain plasticity in the etiology of ASD, Kobayashi et al. (2015) linked this feature to circadian gene pathways. His team showed, in clock-deficient mice, that clock genes intrinsic to PV+ interneurons coordinate postnatal maturation of cells, and consequently, the onset of critical periods of plasticity. Clock-deficient mice exhibited delayed onset of these critical periods despite
having a normal systemic circadian rhythm. This delay was rectified by the pharmacological enhancement of GABAergic transmission (Kobayashi et al., 2015). As highlighted earlier, activity of CLOCK-BMAL1 is tightly linked to environmental conditions. In this way, some environmental conditions, such as sleep deprivation, can impact the timing of critical periods of plasticity and disturb neurodevelopment. A few days of circadian rhythm disorganization can be enough to impact the maturation and specialization of certain brain structures during specific developmental periods, and therefore have a cascade effect on several brain functions (Butt et al., 2017; Charrier et al., 2017).

**VERY EARLY SLEEP ISSUES AND COGNITIVE FUNCTIONS**

If the hypothesis of a direct implication between the alteration of circadian rhythms on ASD etiology is seductive, the complementary (and potentially mutually reinforcing) “sleep disorder bias” must not be disregarded. As mentioned above, sleep issues occur early on in the life of an ASD individual and are proposed as a predictive risk factor for developing ASD (Nguyen, Murphy, Kocak, Tylavsky, & Pagani, 2018). It is therefore difficult, if not impossible, to propose a unique etiology, as sleeping issues may also have a strong impact on cognitive function and may lead to autistic symptoms. In fact, sleep disturbances significantly impact the daily functioning of individuals, affecting their cognitive resources and altering their abilities to regulate their emotions and behaviors (Maruani et al., 2019). Several studies describe the relationship between poor sleep duration or quality, and an alteration of cognitive functions such as executive functions (Astill, Van der Heijden, Van IJzendoorn, & Van Someren (2012)).

Longitudinal studies assessing early life sleep duration and their impact on development exposed the dramatic consequences of sleep disorders. To illustrate, Smithson et al. (2018) found that short sleepers between birth and two years of age had a 5.2-points lower cognitive development score at two years of age compared to intermediate and long sleepers. Regarding language development, short sleepers between two and six years of age present poor receptive vocabulary at ages between six and ten (Seegers et al., 2016). Tomisaki et al. reported an association between proper development of social competence with short sleep onset and sufficient sleep duration in early life (Tomisaki et al., 2018). Similarly, (Weisman, Magori-Cohen, Louzoun, Eidelman, & Feldman, 2011) showed that infants whose sleep-wake transitions were more organized (mainly characterized by shifts between quiet sleep and wakefulness) exhibited the most favorable development, including greater neonatal neuromaturation, less negative emotionality, better cognitive development, and better verbal, symbolic, and executive competences at five years of age.

Even more concerning, insufficient sleep during the first few years of life may have long-standing consequences. It was found that high hyperactivity scores at age six were strongly associated with a pattern of short sleep duration at two and a half years of age, even in children showing normative sleep in the interim period (from three and a half to six years of age). Inconsistent sleep–wake cycles during early development might be contributing to the steadily rising rates of emotional and behavioral problems in young children (Touchette et al., 2007; Touchet, Petet, Tremblay, & Montplaisir, 2009). Thus, it is tempting to speculate that early sleep disorders could lead to autistic symptoms and neurodevelopmental disorders. In a “cascade” model, those symptoms are further exacerbated by persisting sleep difficulties. In addition, many studies outlined the fact that sleep problems tend to compound autism symptomatology and repetitive or aggressive behavior in individuals diagnosed with ASD. [For a review, see (Cohen, Conduit, Lockley, Rajaratnam, & Cornish, 2014)]
Consequently, dysregulation of the circadian system and consequent sleep disorders are being increasingly recognized as aggravating factors in ASD etiology. In regard to recent scientific knowledge, circadian time and ASD seem to be involved in a bidirectional manner one reinforcing the other. Either way, assessing and acting on the circadian pathway by promoting efficient sleep/wake patterns in early life may be central to the treatment of the condition. For future studies, controlling the quality and duration of sleep is mandatory, as the association between circadian rhythm dysfunction and the reported clinical symptoms could be explained by a lack of sleep.

TIME THEORY, A GUIDE TO NEW THERAPEUTIC PERSPECTIVES

Evaluating time processing among children with ASD is the first step in reeducation. In this perspective, some research teams evaluated a time processing training program. Since very few studies involved interventions in ASD individuals, we also reported studies concerning individuals with Attention Deficit/Hyperactivity Disorder (ADHD) or Intellectual Disability (ID). Both neurodevelopmental disorders are often comorbid with ASD (American Psychiatric Association, 2013), and are also associated with difficulties in time perception or management (American Psychiatric Association, 2013; Sharp, Murray, McKenzie, Quigley, & Patrick, 2001; Toplak et al., 2006).

TRAINING AND COMPENSATION OF TIME PERCEPTION

Wennberg et al., who worked on the KaTid, tested a 12-week time processing training program on children with ADHD, across the ages of nine to 15 years old (Wennberg et al., 2018). Three to four treatment sessions, lasting 30 minutes each, focused on finding compensating strategies for the child, structuring the physical environment and identifying adequate time assisting devices. These devices could be alarm clocks, weekly schedules or step-by-step-schedules with text or pictures, and timers representing time visually. Remediation techniques were also used and involved training time perception, orientation and management through the completion of tasks (e.g. assessing the time necessary to complete five daily activities and then identifying which activity could fit within a 45-minute interval, etc.). After 24 weeks, results showed a higher score increase across all exercises of the KaTid program (except for the Time Management dimension) for the treatment group compared to the control group (with 12 weeks of intervention and 12 additional weeks for favoring the use of learned techniques in the everyday environment). The Parent Scale also showed a significant improvement, but not the Time S self-rated questionnaire.

Another method of intervention is derived from the My Time program (Aberg, 2012). It includes five steps: examine, visualize, document, process and discuss. The first step involves focusing on the duration of activities that are of interest to the child and associated experiences. Time is measured using a special quarter-hour stopwatch that makes time visible in the form of dots that fill-in at 15-minute intervals. Only four dots are displayed, which facilitates the understanding and communication of time duration for people who have difficulty with calculations, including those with an intellectual development disorder. The child documents the duration of each measured activity in a time book, drawing black dots. When documentation is completed, differences in duration can be experienced and processed through exercises or playful activities of various durations. and he documented activities are then discussed (e.g., how two activities take the same number of black dots even though their durations feel subjectively different). One study assessed the efficacy of this intervention on children with mild to moderate intellectual disabilities (Gunnel Janeslätt, Ahlström, & Granlund, 2019).
Results showed better improvement in time perception after eight weeks of intervention, compared to the group with no intervention, as assessed by the KaTid. No effect was found on the Parent Scale.

Other time devices have been evaluated in small population studies: the timer software (the Tic Tac tool) which represents the passing of time intervals visually (Campillo et al., 2014) but also the quarter hour watch, the time rule (Arvidsson & Jonsson, 2006), the Time Timer (Grey, Healy, Leader, & Hayes, 2009) or visual calendars (Koyama & Wang, 2011). Different beneficial outcomes were reported, either related to time (regulating the duration of their activities, observing an appointment) or to autism severity (impulsivity, stereotypies). Some teams also propose to use music as a rhythmic temporal reference (Hardy & LaGasse, 2013).

These time reeducation activities should be offered as early as possible during children’s development in order to favor a typical brain maturation during critical developmental stages. Such early intervention may positively impact the emergence of higher-level functions based on time processing.

**RESYNCHRONIZING**

Another way to improve time processing in children with ASD is to help the synchronization of their internal clock. As a first-line treatment, parent-directed behavioral sleep interventions are recommended. These interventions educate parents about sleep hygiene and behavioral responses to their child’s sleep problems and help restoration of a physiological sleep rhythm (Cuomo et al., 2017; Gringras, Nir, Breddy, Frydman-Marom, & Findling, 2017). Attention to circadian synchronizers (or so called zeitgebers) is also crucial. As reported previously, the internal clock needs to be guided by external factors in order to be well synchronized. A good balance of daylight and darkness, regular meal times and physical activity are needed to reinforce internal clock synchronization (Gringras et al., 2017; Logan & McClung, 2019).

When sleep hygiene and behavioral intervention are insufficient, supplementation in melatonin could be offered. Melatonin treatment has been evaluated in several small studies with promising efficiency for sleep issues, and also has beneficial effects on autism severity (for a review see Tordjman et al., 2015).

More recently, pediatric prolonged-release melatonin has been evaluated in a larger population. The long- and short-term efficacy of pediatric prolonged-release melatonin has been reported on total sleep duration, sleep latency and quality of life, with satisfying safety and good acceptability of treatment (Gringras et al., 2017; Maras et al., 2018). A decrease in externalizing behavior (i.e. aggressive behaviors) as well as an increase in family quality of life was also reported (Schroder et al., 2019). This could be a promising step to regulate circadian rhythm early in the development of ASD individuals where this process is altered, as well as its associated symptoms.

In a different way, time remediation may be “naturally” included in some global developmental and early relational intervention, such as the Early Start Denver Model (ESDM) or more communication focused intervention, such as Pediatric Autism Communication Therapy (PACT) (Dawson et al., 2010; Green et al., 2010). These therapies have the common aim of establishing dyadic, sustained and synchronized interactions between ASD toddlers and their caregivers, in order to improve the toddler’s reciprocal social interaction skills. Because such interventions increase the opportunities for the child to integrate multisensory social stimuli and to adjust one’s behavior in synchrony to others’ cues, i.e.
two main features associated with time perception, we should expect an improvement of time perception, as well, in such children.

DISCUSSION

There is growing evidence of impaired time processing in ASD compared to TDC no matter the evaluated “time level.” This review is the first to gather information about time processing and management across the time spectrum. Different scientific fields have been covered here to allow a global view of time processing and management impairments in ASD.

Time interval perception is likely to be impacted by atypical cognitive strategies which involve attentional network and short-term memory capacity and is dependent on sensory modalities. So far, individuals with ASD seem to be efficient in measuring time through visual cues, with preserved-to-enhanced visual, but not auditory, time processing abilities. In the same way, multimodal temporal integration is impaired in ASD with difficulties concerning audio-visual integration. This has been linked to socio-communication impairment. Along these lines, alterations of circadian pathway have been found on multiple levels; from genetic dysregulation to biological imbalance and behavioral features, circadian pathway and ASD are involved in a bidirectional manner, one reinforcing the other.

A neurodevelopmental point of view with a cascading effect of “temporal processing” impairment on higher-level cognitive skills, is adopted in recent scientific literature as millisecond, interval and circadian timing are entangled in many crucial functions. A small defect in these processes could have a cascading effect on development, and lead to, or worsen, symptoms of autism. Resulting from correlations or mediation analysis, this hypothesis needs longitudinal studies to be validated, as none has been found within this literature review.

There is a lack of information concerning the interdependence of the different “time systems” (i.e. millisecond, interval or circadian timing) and global explaining models are only speculative; future studies should assess time processing at multiple levels while taking care of essential confounding factors such as developmental age, symptom heterogeneity, cognitive functions, comorbidities or medication. Multidisciplinary approaches could be of great use to allow the concomitant exploration of the severity of autistic symptoms, time perception and biological rhythms. Electronic devices could be the support of some “time” assessment such as sleep/wake rhythm or time perception tasks. This could improve the feasibility of multidisciplinary studies at a higher scale in space, but also in time!

To conclude, this review shows that it would be highly relevant to systematically assess temporal perception and processing in ASD, and to add this data to global functional assessments before intervention. The reeducation of time perception as well as resynchronization of circadian rhythms could consistently improve ASD symptoms. This knowledge may also guide parents to better help their children on a daily basis with simple advice, such as the use of visual aids are used to help ASD individuals to better represent time intervals and schedules, but also by promoting essential behavior such as efficient sleep/wake patterns in early life.

AUTHORS’ CONTRIBUTIONS
L. J. screened the articles, made the table, contributed to the writing of the discussion and wrote the “circadian” part.

Y. L. wrote the introduction and the “millisecond and interval timing” part and participated in minor editing throughout other sections of the paper.

M. B. mainly contributed to the writing of the “Assessing time perception in autistic patients” and participated in minor editing throughout other sections of the paper.

A. E. participated in rereading and in editing throughout the manuscript.

V. S. participated in rereading and in editing throughout the manuscript.

M. D. participated in rereading and in editing throughout the manuscript.

MM. G. participated in rereading and in editing throughout the manuscript and contributed to the writing of clinical overview.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare.
BIBLIOGRAPHIE


Panda, S., Hogensch, J. B., & Kay, S. A. (2002). *Circadian rhythms from flies to human.* https://doi.org/10.1038/417329a


of parvalbumin in mice leads to behavioral deficits relevant to all human autism core symptoms and related neural morphofunctional abnormalities. *Translational Psychiatry, 5*(3), e525–e525. https://doi.org/10.1038/tp.2015.19

### ANNEXES 1. TABLE 1.

<table>
<thead>
<tr>
<th>Article</th>
<th>Population</th>
<th>Mean Age (ASD/TD)</th>
<th>Mean IQ (ASD/TD)</th>
<th>Modality</th>
<th>Time range</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Szeland, 2004</td>
<td>7 ASD/7 TD</td>
<td>12.6 / ?</td>
<td>PIQ 82-102/95-145</td>
<td>Visual/Auditive</td>
<td>1000-5500ms</td>
<td>DR: overestimation of longer duration, underestimation of shorter duration in ASD group</td>
</tr>
<tr>
<td>Wallace, 2008</td>
<td>25 ASD/25 TD (including 4 D)</td>
<td>14.10 / 13.84</td>
<td>FSIQ 96.36/100.08</td>
<td>None?</td>
<td>2-45s</td>
<td>DDT: n.s. DR: n.s.</td>
</tr>
<tr>
<td>Jones, 2009</td>
<td>72 ASD/52 TD</td>
<td>15.6 / 15.6</td>
<td>FSIQ 88/89 PIQ 93/93 VIQ 84/87</td>
<td>Auditive</td>
<td></td>
<td>DDT: n.s.</td>
</tr>
<tr>
<td>Martin, 2009</td>
<td>20 ASD/20 TD</td>
<td>36 / 35</td>
<td>FSIQ 106/108 PIQ 105/106 VIQ 107/108</td>
<td>Auditive</td>
<td>0.5 – 4.1s</td>
<td>DR: ASD group less accurate with an increase variability</td>
</tr>
<tr>
<td>Allman, 2011</td>
<td>13 ASD/12 TD</td>
<td>10.3 / 10.3</td>
<td>VIQ 100 / ?</td>
<td>Visual</td>
<td>1-8s</td>
<td>TBT: ASD experienced greater difficulty discriminating between longer durations, less accurate, decrease sensibility to duration</td>
</tr>
<tr>
<td>Maister, 2011</td>
<td>21 ASD/21 TD and 15 ASD/15 TD</td>
<td>11.3/10.7 and 11.8/11.2</td>
<td>RPM 40/38 and 40/40</td>
<td>Visual</td>
<td>0.5-45s</td>
<td>DR: lower performances in ASD group for shorter and longer durations, increased intraindividual variability</td>
</tr>
<tr>
<td>Falter, 2012</td>
<td>18 ASD/19 TD</td>
<td>25.3 / 26.1</td>
<td>FSIQ 112/113</td>
<td>Visual/Auditive</td>
<td>600-1000ms</td>
<td>DDT: lower sensitivity to duration in ASD group in both modalities, with better results in visual modality Lower performance are correlated to severity of communication impairment</td>
</tr>
<tr>
<td>Study</td>
<td>Participants</td>
<td>Duration</td>
<td>FSIQ</td>
<td>WMI</td>
<td>PSI</td>
<td>Type</td>
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<tr>
<td>Gil, 2012</td>
<td>12 ASD / 12 TD</td>
<td>9-17 / 8-16</td>
<td>FSIQ 94.37 / 101.45</td>
<td>WMI 91.37 / 100.81</td>
<td>PSI 83.25 / 101.45</td>
<td>visual</td>
</tr>
<tr>
<td>Bhatara, 2013</td>
<td>12 ASD / 15 TD</td>
<td>10-14</td>
<td>VIQ 71-123 / 81-126</td>
<td>PIQ 79-136 / 75-129</td>
<td></td>
<td>auditive</td>
</tr>
<tr>
<td>Brodeur, 2014</td>
<td>15 ASD / 15 TD</td>
<td>10.16 / 6.61</td>
<td></td>
<td>mental age : 6.19 / 6.22</td>
<td></td>
<td>auditive</td>
</tr>
<tr>
<td>Brenner, 2015</td>
<td>27 ASD / 25 TD</td>
<td>12.68 / 13.41</td>
<td>FSIQ 101.31 / 106.96</td>
<td></td>
<td></td>
<td>visual</td>
</tr>
<tr>
<td>Karaminis, 2016</td>
<td>23 ASD / 78 TD</td>
<td>7.9–14.8 / 7.8–13.10</td>
<td>FSIQ 100.3</td>
<td></td>
<td></td>
<td>visual</td>
</tr>
<tr>
<td>Foss-Feig, 2017</td>
<td>26 ASD / 27 TD</td>
<td>11.94 / 11.93</td>
<td>FSIQ 115.96 / 114.5</td>
<td></td>
<td></td>
<td>auditive and visual</td>
</tr>
<tr>
<td>Jones, 2017</td>
<td>20 ASD / 26 TD</td>
<td>45.4 / 44.0</td>
<td>PIQ 110 / 105.6</td>
<td>FSIQ 114.6 / 108.1</td>
<td></td>
<td>visual (with an emotional component)</td>
</tr>
<tr>
<td>Lambrechts, 2017</td>
<td>18 ASD / 18 TD</td>
<td>25.3 / 26.4</td>
<td>VIQ 110 / 113</td>
<td>PIQ 112 / 116</td>
<td>FSIQ 112 / 116</td>
<td>auditive</td>
</tr>
<tr>
<td>Study</td>
<td>Participants</td>
<td>Criteria</td>
<td>Scores</td>
<td>Modality</td>
<td>Timing Threshold</td>
<td>DDT</td>
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<tr>
<td>Isaksson, 2018</td>
<td>17 ASD / 18 TD</td>
<td>11 / 10.4</td>
<td>FSIQ 102 / 109</td>
<td>Auditive</td>
<td>200-2000ms / 1.5min (verbal duration estimation)</td>
<td>- significant difference between groups for sub-second durations (threshold higher in ASD, poorer performances)</td>
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<tr>
<td>Lukito, 2018</td>
<td>23 ASD / 25 ADHD / 24 ASD+ADHD / 26 TD</td>
<td>23 / 23.1 / 22.9 / 23.4</td>
<td>FSIQ 103.7 / 116 / 106.9 / 117.3</td>
<td>Visual</td>
<td>1000-1500ms</td>
<td>DDT: n.s.</td>
</tr>
<tr>
<td>Salunkhe, 2018</td>
<td>40 TD / 20 ADHD / 20 ADHD + ASD</td>
<td>10.23 / 10.79 / 9.98</td>
<td>FSIQ 107.20 / 109.10 / 103.95</td>
<td>Visual</td>
<td>1, 2, 4, 8, or 16 s</td>
<td>DR:</td>
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<tr>
<td>Steward, 2018</td>
<td>24 students: AQ score</td>
<td>22.3</td>
<td>RPM 21</td>
<td>Auditive</td>
<td>300, 360, 420, 480, 560 or 600 ms</td>
<td>DDT: correlation between timing threshold and AQ score (the more the AQ the higher the threshold, the poorer the performance)</td>
</tr>
<tr>
<td>Edey, 2019</td>
<td>25 - 24 ASD / 24 - 22 TD</td>
<td>38.2 - 35.4 / 33.8 - 32.7</td>
<td>FSIQ 112.6 - 114.57 / 108 - 108.6</td>
<td>Auditive then visual</td>
<td>300, 400, 500, 600, 700, 800, 900 ms</td>
<td>DDT:</td>
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</table>

Table 1. Studies of time perception (duration, reproduction and bisectional task) in ASD compared to TD. FSIQ = Full Scale Intellectual Quotient, WMI = Working Memory Index, RPM = Raven's Progressive Matrices, PIQ = Performance Intellectual Quotient, VIQ = Verbal Intellectual Quotient, n.s. = non significant